# Contextual stress and physical environmental toxins linked to urban childhood asthma: Independent and synergistic effects

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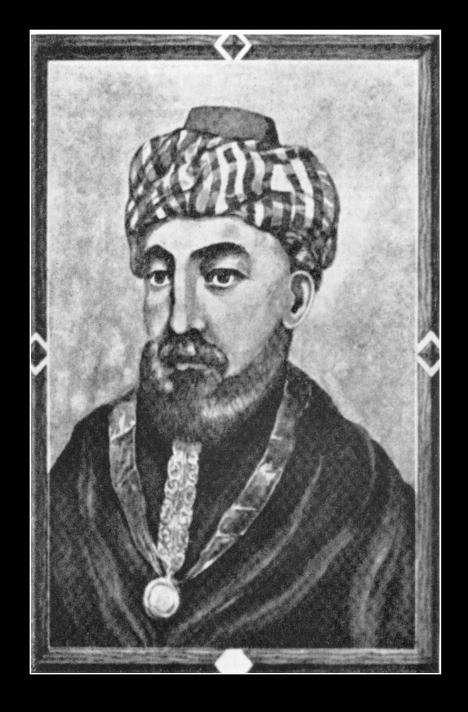
Boston, MA





### The Natural History of Asthma Genetic **Factors REMISSION** (Atopy) Viruses Relapse or Disease Wheezing **ASTHMA Progression** Family hx of asthma Passive smoke exposure **Atopic disease New Onset Allergens Inflammation and Remodeling**

Borrowed from Lemanske R.



Noted that mental suffering impairs physical well-being and adversely affects the respiratory organs; and this was universally known in the 12th century

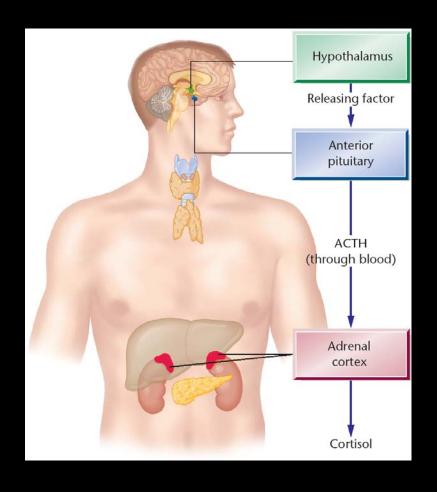
..' the success of relieving the patient depends largely on an intimate knowledge of the *total* patient."

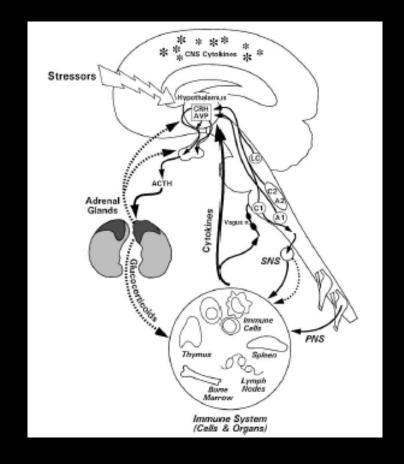
Treatise on Asthma

Maimonides Rabenu Moshe Ben Maimon (1135 - 1204)



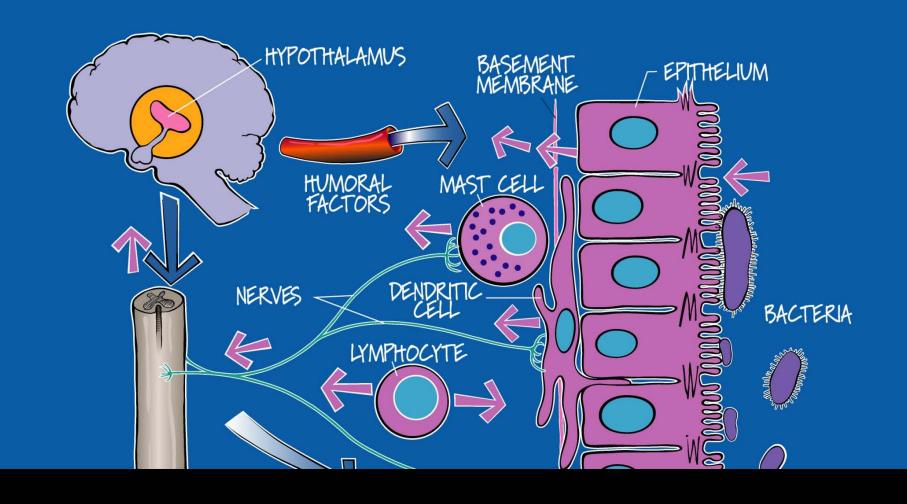
### **Neuroendocrine - Immune Interactions**





- Sympathetic-Adrenomedullary (SAM) System
- •Hypothalamic-Pituitary-Adrenocortical (HPA) System

These systems are regulated in the brain



Wright et al., Thorax 1998; 53:1066-74
Wright et al., JACI 2005; 5:23-9
Wright RJ, Bio Rsychol 2010 [Elbub ahead of print

SPINAL COR

### Materno-fetal interaction in pregnancy

### Mother

Maternal allergic phenotype (direct non-genomic effects)

- Antibodies
- · Cellular transfer
- Cytokine mikieu



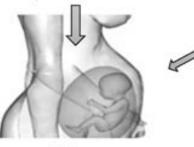
In utero effects

Perinatal effects

Postnatal effects

Ohter endogenous factors (which may affect cytokine milieu)

· Stress/HPA activation



#### Fetus

- · Fetal genotype
- · Predisposing polymorphisms
- Gender



- · Delivery method (caesaream)
- · Perinatal antibiotics
- · Other perinatal events



- Colonisation
- · Breastfeeding
- · Infant diet (immunomodulatory nutrients/allergens)
- · Smoking and other pollutants

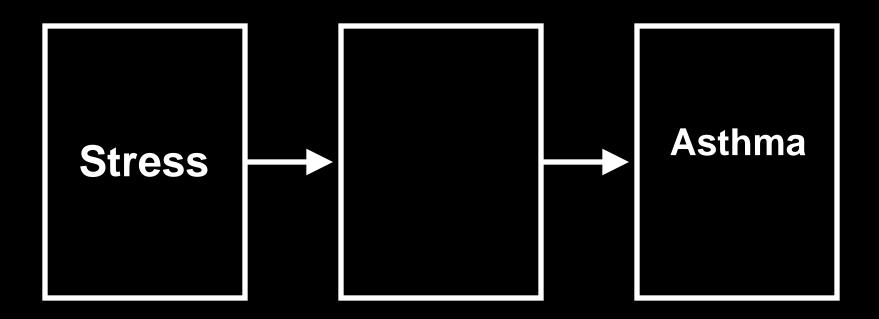


Disease predisposition

### Maternal environment (exposures in pregnancy)

- · Microbial burden
- · Smoking and other pollutants
- Medications
  - Antacids,
  - Paracetamol
  - Antibiotics
- · Dietary factors
  - Folate
  - LC-PUCA
  - Antioxidants
  - Vitamin D

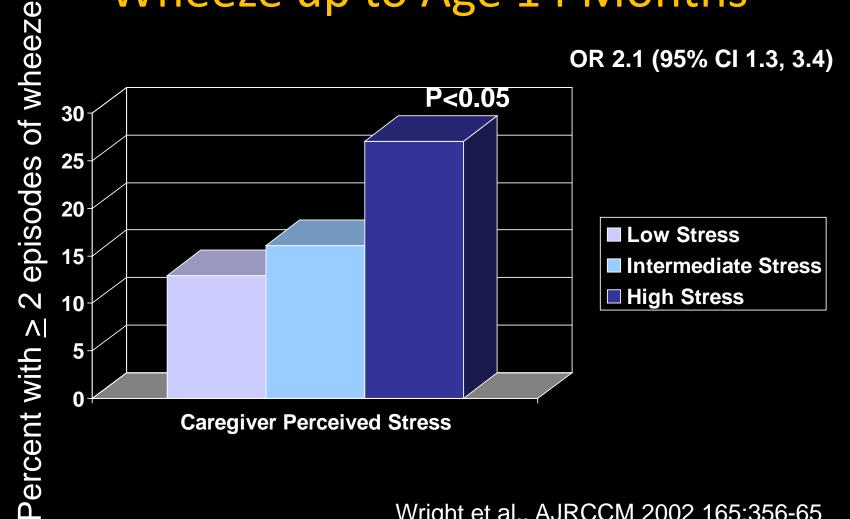
## Black Box Model of Stress and Asthma Epidemiology



Can differential life stress experiences contribute to health disparities?



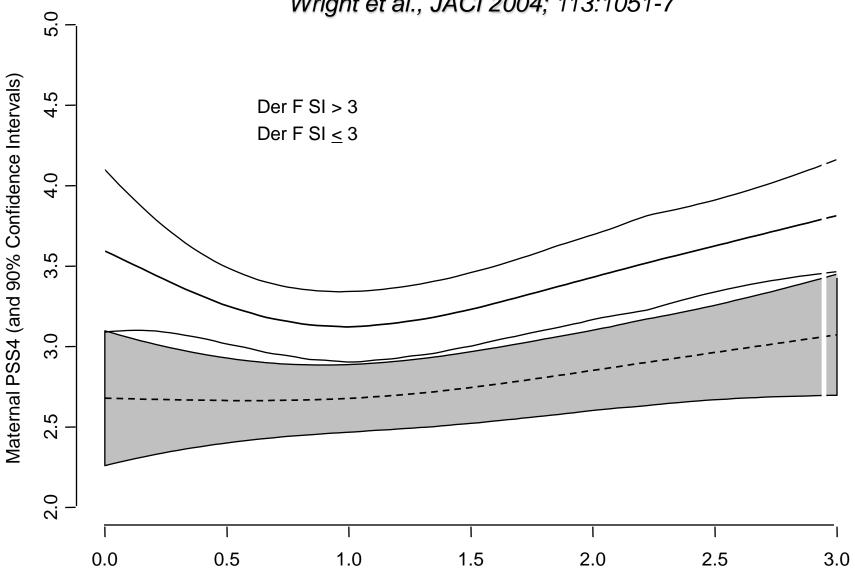
## Caregiver Stress and Repeated Wheeze up to Age 14 Months



Wright et al., AJRCCM 2002 165:356-65

### Mean Caregiver Stress Over Time: Comparing High to Low Lymphocyte Proliferative Response to Der f 1

Wright et al., JACI 2004; 113:1051-7



Child's Age (Years)
Analysis also controls for race, active maternal asthma, and cold status.



Air Pollution

Tobacco Smoke

NIEHS, NICHD, NHLBI, NIMH



**Stress** 

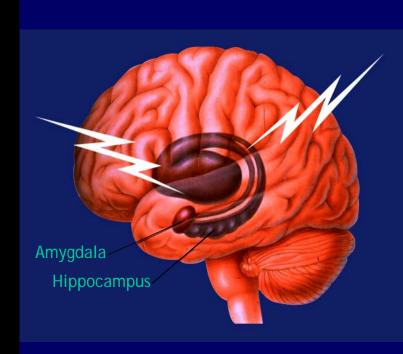
Allergens

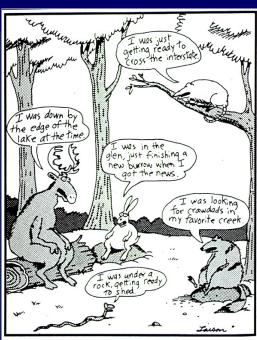
### Stress is Normative

- At some point, we all encounter major life stress, and daily we manage more minor stress
  - Daily hassles
    - Late for appointment, no parking space, elevator slow to arrive....
  - Chronic Stress
    - Constant money worries, marital problems, caring for chronically ill spouse or child....
  - Major Life Stress
    - Death of loved one, break up of significant relationship, serious accident, natural disaster

### Trauma – Candidate Stressor Not normative

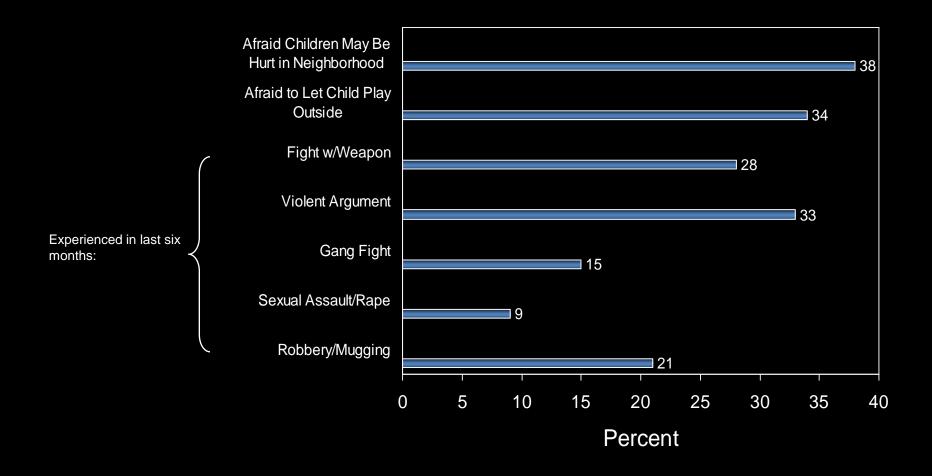
### Memory - Strong Emotions





More facts of nature: All forest animals, to this very day, remember exactly where they were and what they were doing when they heard that Bambi's mother had been shot.

### Caretaker Exposure to Violence (ICAS)



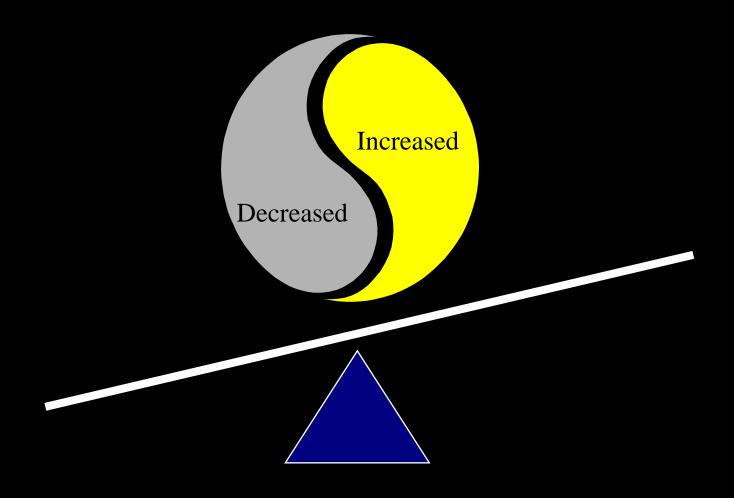


**Children Reflect What They See - ?physiologically** 

### **Stress Domains**

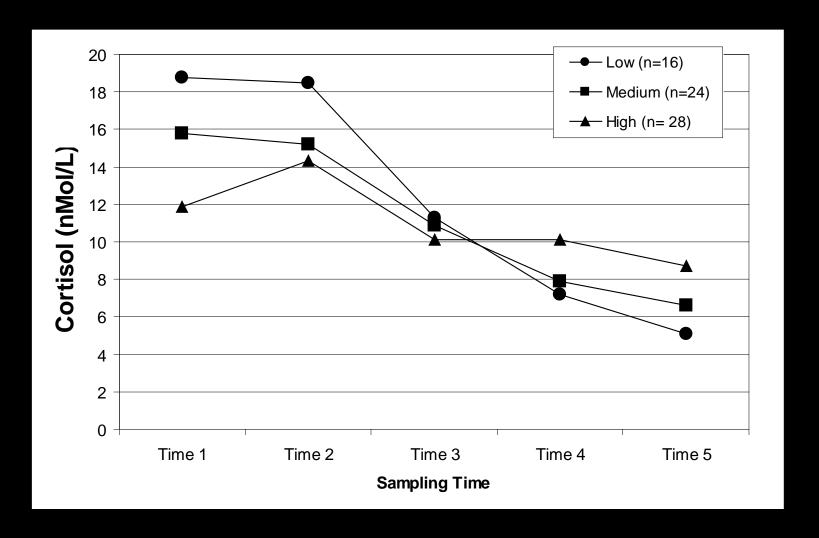
- Financial strain
- Racism/discrimination
- Interpersonal violence
- Community violence
- Other negative life events (housing, landlords, fear of eviction, etc.)

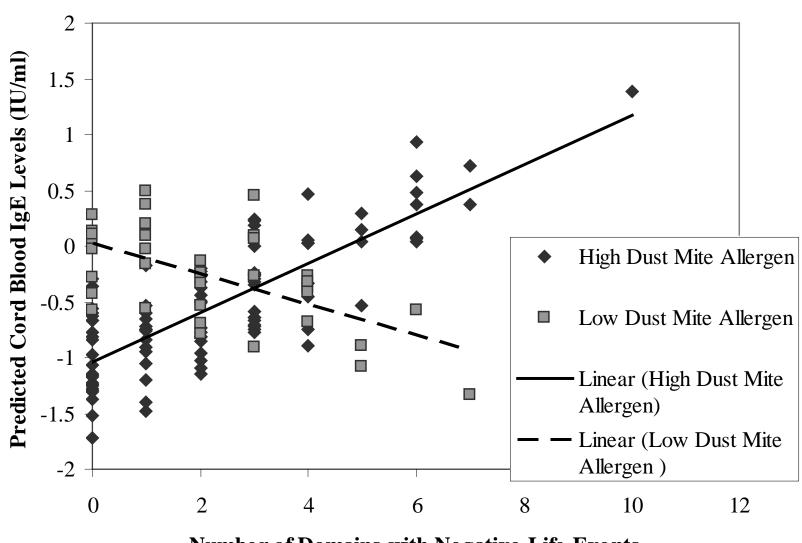
## Cortisol in Health and Disease



**Stress is an endocrine disruptor** 

## **Preliminary Cortisol Analyses**

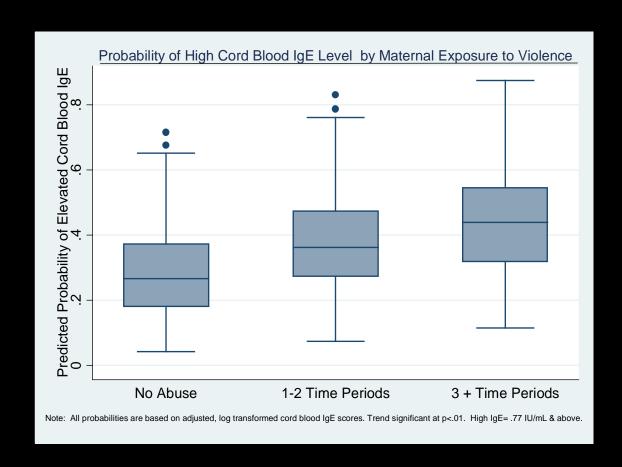




**Number of Domains with Negative Life Events** 

### Maternal interpersonal trauma and cord blood IgE levels in an inner-city cohort: A life-course perspective

Michelle Judith Sternthal, PhD,<sup>a</sup> Michelle Bosquet Enlow, PhD,<sup>b</sup> Sheldon Cohen, PhD,<sup>c</sup> Marina Jacobson Canner, MA,<sup>d</sup> John Staudenmayer, PhD,<sup>e</sup> Kathy Tsang, MHA,<sup>d</sup> and Rosalind J. Wright, MD, MPH<sup>a,d</sup> Boston and Amherst, Mass, and Pittsburgh, Pa



Sternthal et al., JACI 2009; 124:954-60

## During early childhood the human stress system is under strong social regulation

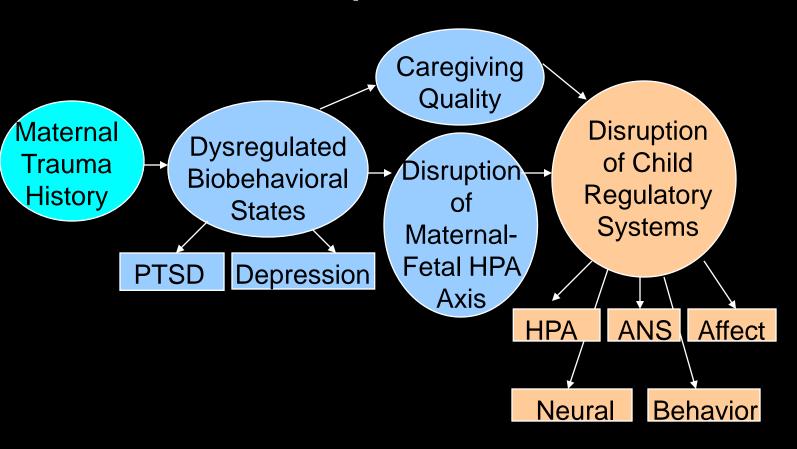


As quality of care decreases, young children become highly stress vulnerable

Sensitive, responsive, supportive care "buffers" or protects young children from experiencing elevated stress hormone levels



## Specific Model



## Sample

- 50 mother-infant dyads to date
  - primarily low-income
  - racial/ethnic background

	White	Black	Asian	Multi-racial
Non-Hispanic	18%	36%	4%	8%
Hispanic	20%	6%	0%	8%

- From Project ACCESS (PI RJ Wright)
- Lifetime trauma exposure
  - $-84\% \ge 1$  Criterion A event(s)
    - consistent with studies with similar samples
  - M = 2.7 events, range 0-10
  - large majority prior to pregnancy

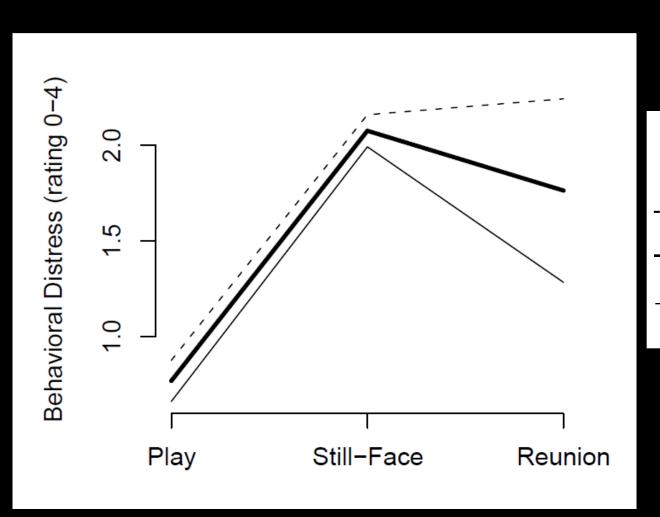
## LifeShirt System: Autonomic Reactivity



## Dyadic Regulation

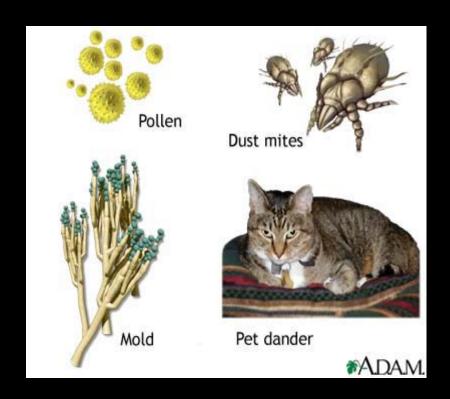
- Still-Face Paradigm (SFP)
  - standardized dyadic stressor (Tronick et al., 1978)
- Repeated version (2 min each)
  - Play (baseline)
  - Still-Face 1 (stressor)
  - Reunion 1 (recovery)
  - Still-Face 2 (stressor)
  - Reunion 2 (recovery)

## SFP: Infant Distress Recovery



Maternal Lifetime
Trauma Exposure
----- High Exposure
--- Moderate Exposure
--- Low Exposure

## Is Environmental Control Helpful?

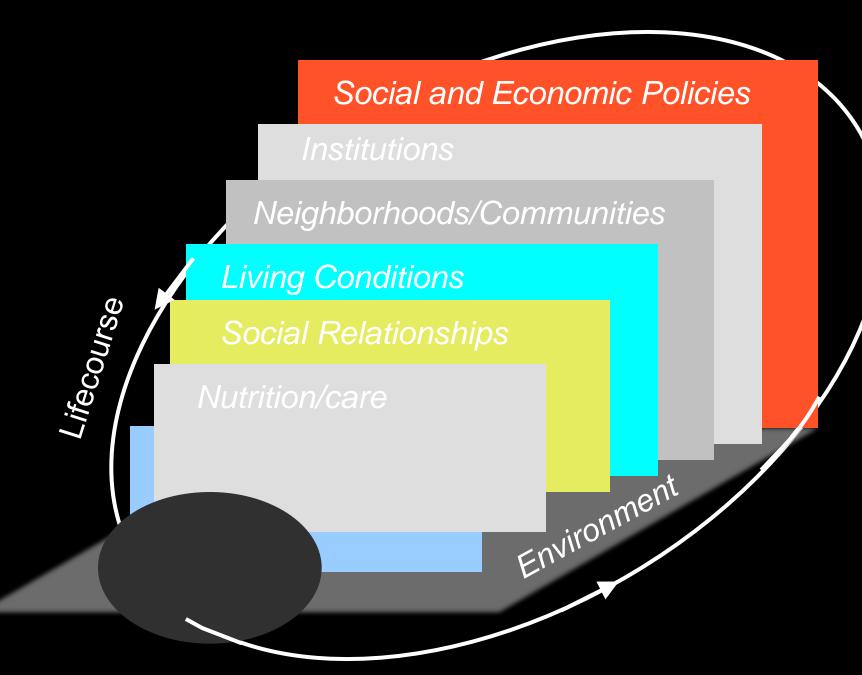


http://health.allrefer.com/health/asthma-common-asthma-triggers.html

## Why not stress management?

- 1. Meditation
- 2. Laugh Out Loud
- 3. Play Soothing Music
- 4. Think Happy Things
- 5. Take a Short Walk
- 6. Slow/Deep Breaths
- 7. Relax Body(Before/After Bed)





### Collaborators

### **Channing Laboratory**

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### **Boston Children's**

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**Sheldon Cohen** 

### **SMU**

**Thomas Rtiz** 





